

**REMARKS****A. Status of the Claims**

In Applicants' previous paper, Applicants elected to prosecute Group I, which corresponds to claims 51-55, 64-73, 77-118, 146, 149, and 150. In this paper, Applicants have requested the cancellation of claims 52, 74-76 and 118-145. In addition, Applicants have added new claim 151. Accordingly, the only claims currently pending in this case and presented for examination are claims 51, 53-55, 64-73, 77-117, 146, 149-151. Applicants further note that all claim cancellations are made without prejudice or disclaimer, and Applicants reserve the right to file divisional applications to pursue the cancelled subject matter.

The Office Action rejects claims 51 and 116-118 under 35 U.S.C. §112, ¶2 for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Office Action provisionally rejects claims 51-55, 63-73, 77-85, 11, 149, and 150 on the ground of non-statutory obviousness-type double patenting for allegedly being unpatentable over claims 78-85, 88, and 90-97 of co-pending U.S. Appln. No. 10/591,485. The Office Action also provisionally rejects claims 51, 54, 55, 77, 80-87, 97, 98, 149, and 150 on the ground of non-statutory obviousness-type double patenting for allegedly being unpatentable over claims 1-5, 10 and 11 of co-pending U.S. Appln. No. 12/647,677.

Claims 51-55, 64-73, 77-118, 146, 149, and 150 are rejected under 35 U.S.C. §102(c) for allegedly being anticipated by U.S. Pre-Grant Publication No. U.S. 2004/0220100 to Waugh et al. ("Waugh '100").

Claims 51-55, 77, 80, 81, 86-93, 97-104, 110-115 and 118 are rejected under 35 U.S.C. §102(e) for allegedly being anticipated by U.S. Pre-Grant Publication No. U.S. US2003/0229034 to Waugh et al. (“Waugh ‘034”).

Claim 117 is rejected under 35 U.S.C. §103(a) for allegedly being unpatentable over Waugh ‘034, in view of U.S. Patent No. 6,688,311 to Hanin (“Hanin”), and Waugh ‘100.

Claims 64-73, 78, 79, 82-85, 94-96, 105-109, 116, 149, and 150 are rejected under 35 U.S.C. §103(a) for allegedly being unpatentable over Waugh ‘034 in view of Hanin.

In addition, the Office Action objects to the specification and claims for various informalities, as discussed and addressed below.

#### B. Explanation of the Amendments

Claim 51 has been amended to recite “positively charged efficiency groups.” Support for this amendment is found, for example, in paragraph [0036] of the originally filed specification (i.e., International Application PCT/US2005/007524). Similar amendments have been made to dependent claims 92 and 94-96 in order to maintain consistency in the claim language.

Claim 51 has also been amended to specify that the “carrier and the botulinum toxin non-covalently and directly associate.” Support for this amendment is found, for example, at paragraph [0032], which states that “in all aspects of the present invention, the association between the carrier and the biologically active agent is by non-covalent interaction, non-limiting examples of which include ionic interactions, hydrogen bonding, van der Waals forces, or combinations thereof.” Support is also found at paragraph [0047] of the original specification, which discloses that the positively charged backbone carriers of the invention form complexes with the botulinum toxin. Support is also found in paragraph [0050], which states that botulinum

toxin from certain sources may have a lower propensity for complexation with the positively charged backbones of the invention, which implies that botulinum toxin has a propensity to associate directly with the positively charged backbones of the invention to form a complex. Support is also found in paragraph [0064], which states that the examples provided in the specification “demonstrate delivery of functional botulinum neurotoxin complexes across skin without requiring covalent modification of the neurotoxin to be delivered.”

Claim 53 has been amended to correct an informality.

Claims 86, 87, and 93 have been added to include SEQ ID NOs.

Claim 108 has been amended such that it now depends from claim 102.

New claim 151 has been added. Support for this new claim is generally found throughout the specification. See, e.g., ¶[0043], which states that “[t]he botulinum toxin may be any of the botulinum toxin complexes produced by the bacterium...”.

Applicants respectfully submit that no new matter has been added by these amendments.

### C. Objections to the Specification

#### 1. Identification of Amino Acid Sequences in the Specification

The Office Action objects to the specification for failing to identify all amino acid sequences with sequence identifier numbers. As shown in the “Amendments to the Specification” section beginning on page 12 of this response, Applicants have amended the specification to include SEQ ID NOs that correspond to the sequence listing that was filed with this application. Accordingly, Applicants respectfully request reconsideration and withdrawal of objection to the specification.

2. Trademarks in the Specification

The Office Action requests that the specification be amended to capitalize all trademarks and to include generic descriptive terminology as well. As shown in the “Amendments to the Specification” section beginning on page 12 of this response, Applicants have amended the specification as requested by the Office Action. Accordingly, Applicants respectfully request reconsideration and withdrawal of objection to the specification.

D. Objections to the Claims

1. Objection to Claim 53

The Office Action objects to claim 53 for a minor typographical error involving the word “in.” As shown on page 2 of this response, Applicants have amended claim 53 to correct this informality. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection.

2. Claim Objections Based on Sequence Listings

The Office Action objects to the claims for reciting amino acid sequences without sequence number identifiers. As shown on pages 5-7 of this response, Applicants have amended the claims to correct these informalities. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

3. Objections Under 35 C.F.R. §1.74(c)

The Office Action objects to claims 52 and 108 for allegedly failing to further limit the subject matter of a previous claim. In response, Applicants have cancelled claim 52 and have

amended claim 108 such that it now depends from claim 102, rather than 51. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection to the claims.

E. Rejections Under 35 U.S.C. §112

The Office Action rejects claims 51 and 116-118 under 35 U.S.C. §112, ¶2 for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. However, in making this rejection, the Office Action only specifically discusses claim 118 and claim 104. Applicants therefore address the rejections of claims 118 and 104 below, and maintain that claims 51 and 116-117 are not indefinite.

With respect to claim 118, the Office Action states that the phrase “cell-encapsulating device” is vague and indefinite. Without agreeing to the propriety of this rejection, Applicants have cancelled claim 118, thereby rendering this rejection moot.

With respect to claim 104, the Office Action states that there is insufficient antecedent basis for the phrase “in which the polyalkyleneimine is a polyethyleneimine.” Applicants have amended claim 104 such that it depends from claim 103, rather than claim 102. In view of this amendment, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

F. Double Patenting Rejections

The Office Action provisionally rejects claims 51-55, 63-73, 77-85, 11, 149, and 150 on the ground of non-statutory obviousness-type double patenting for allegedly being unpatentable over claims 78-85, 88, and 90-97 of co-pending U.S. Appln. No. 10/591,485. The Office Action also provisionally rejects claims 51, 54, 55, 77, 80-87, 97, 98, 149, and 150 on the ground of

non-statutory obviousness-type double patenting for allegedly being unpatentable over claims 1-5, 10 and 11 of co-pending U.S. Appln. No. 12/647,677.

In response, Applicants respectfully request that these double patenting rejections be held in abeyance, since U.S. Appln. No. 10/591,485 and U.S. Appln. No. 12/647,677 are still under prosecution. Applicants reserve the right to file a terminal disclaimer or to amend the claims, should it become necessary at a later stage of prosecution.

G. Rejections Under 35 U.S.C. §102

1. Rejections Under 35 U.S.C. §102(e) based on Waugh ‘100

Applicants respectfully traverse the rejection of claims 51-55, 64-73, 77-118, 146, 149, and 150 under 35 U.S.C. §102(e) for allegedly being anticipated by Waugh ‘100. Briefly, Waugh ‘100 is not available as prior art under 35 U.S.C. §102(e) because the inventors in Waugh ‘100 are the same as in the present case. Accordingly, 35 U.S.C. §102(e) is not applicable, and the rejection should be withdrawn.

Section 102(e) of Title 35 of the United States Code states, in relevant part, that “[a] person shall be entitled to a patent unless...the invention was described in (1) an application for patent, published under section 122(b), **by another** filed in the United States before the invention by the applicant for patent...”. See, 35 U.S.C. §102(e) (emphasis added). The Court of Appeals has held that the requirement “by another” is met in this context if not all inventors in the cited reference and application at hand are the same. *In re Land*, 368 F.2d 866, 151 USPQ 621 (CCPA 1966).

In this case, the two people named as inventors in the present application are Michael Dake and Jacob Waugh. These are the same people named as inventors in Waugh ‘100, as

shown in the excerpts of bibliographic information shown on the first pages of the respective U.S. Pre-Grant Publications:

(19) **United States**

(12) **Patent Application Publication**  
**Dake et al.**

(10) **Pub. No.: US 2008/0107690 A1**

(43) **Pub. Date: May 8, 2008**

(54) **COMPOSITIONS AND METHODS FOR  
TOPICAL APPLICATION AND  
TRANSDERMAL DELIVERY OF  
BOTULINUM TOXINS**

**Related U.S. Application Data**

(60) Provisional application No. 60/550,015, filed on Mar. 3, 2004.

**Publication Classification**

(76) Inventors: **Michael D. Dake**, Stanford, CA  
(US); **Jacob M. Waugh**, Mountain  
View, CA (US)

(51) **Int. Cl.**  
*A61K 51/00* (2006.01)  
*A61K 39/40* (2006.01)  
*A61K 39/42* (2006.01)

(19) **United States**

(12) **Patent Application Publication**  
**Waugh et al.**

(10) **Pub. No.: US 2004/0220100 A1**

(43) **Pub. Date: Nov. 4, 2004**

(54) **MULTI-COMPONENT BIOLOGICAL  
TRANSPORT SYSTEMS**

(60) Provisional application No. 60/220,244, filed on Jul. 21, 2000.

**Publication Classification**

(75) Inventors: **Jacob Waugh**, Mountain View, CA  
(US); **Michael Duke**, Stanford, CA  
(US)

(51) **Int. Cl.**<sup>7</sup> ..... **A61K 38/17**  
(52) **U.S. Cl.** ..... **514/12**

Accordingly, the invention in Waugh ‘100 was not described “by another,” and 35 U.S.C. §102(e) does not apply. Moreover, no other provision of 35 U.S.C. §102 applies either. For example, Waugh ‘100 is not prior art under 35 U.S.C. §102(a). More specifically, because Waugh ‘100 and the present application share the same inventors, the presently claimed invention was not “known or used by others...” as required to sustain a rejection under 35 U.S.C. §102(a).

In addition, Waugh ‘100 is not prior art under 35 U.S.C. §102(b). The present application is a national phase application corresponding to PCT/US05/07524, which was filed

on March 3, 2005, claiming the benefit to priority to U.S. Provisional Application 60/550,015 filed March 3, 2004. Since Waugh '100 was published November 4, 2004, it was not published "more than one year prior to the date of the application for patent in the United States" as required by 35 U.S.C. §102(b). Furthermore, none of the other subsections of 35 U.S.C. §102 (i.e., §§102(c); 102(d), 102(g), or 102(g)) apply either. Accordingly, Waugh '100 is not available as prior art under 35 U.S.C. §102, and rejection should be withdrawn.

1. Rejections Under 35 U.S.C. §102(e) based on Waugh '034

Applicants respectfully traverse the rejection of claims 51-55, 77, 80, 81, 86-93, 97-104, 110-115 and 118 under 35 U.S.C. §102(e) for allegedly being anticipated by Waugh '034. Briefly, Waugh '034 is not available as prior art under 35 U.S.C. §102(e) because the inventors in Waugh '034 are the same as in the present case. Accordingly, 35 U.S.C. §102(e) is not applicable, and the rejection should be withdrawn.

As noted above, in order for a reference to be prior art under 35 U.S.C. §102(e), the invention must be described in that reference "by another." *See*, 35 U.S.C. §102(e). Jacob Waugh and Michael Dake are the named inventors on the present case, as well as Waugh '034, as shown by the following excerpts of the bibliographic pages of these two U.S. Pre-Grant publications.

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2003/0229034 A1**  
Waugh et al. (43) **Pub. Date: Dec. 11, 2003**

(54) **MULTI-COMPONENT BIOLOGICAL  
TRANSPORT SYSTEMS**

**Related U.S. Application Data**

(75) Inventors: **Jacob Waugh**, Millbrae, CA (US);  
**Michael Dake**, Stanford, CA (US)

(60) Provisional application No. 60/220,244, filed on Jul.  
21, 2000.

**Publication Classification**



(19) **United States**(12) **Patent Application Publication**  
**Dake et al.**(10) **Pub. No.: US 2008/0107690 A1**  
(43) **Pub. Date: May 8, 2008**(54) **COMPOSITIONS AND METHODS FOR  
TOPICAL APPLICATION AND  
TRANSDERMAL DELIVERY OF  
BOTULINUM TOXINS****Related U.S. Application Data**(60) Provisional application No. 60/550,015, filed on Mar.  
3, 2004.(76) Inventors: **Michael B. Dake**, Stanford, CA  
(US); **Jacob M. Waugh**, Mountain  
View, CA (US)**Publication Classification**(51) **Int. Cl.**  
**A61K 51/00** (2006.01)  
**A61K 39/40** (2006.01)  
**A61K 39/42** (2006.01)

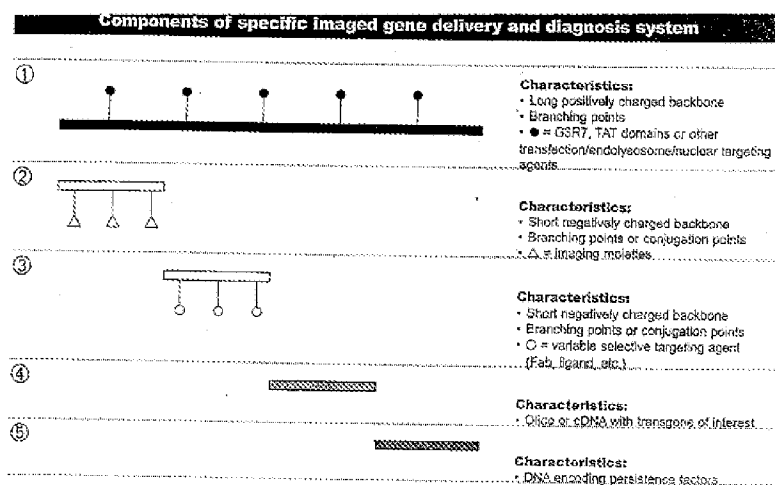
Thus, like Waugh '100, Waugh '034 does not qualify as prior art under 35 U.S.C. §102(e).

Additionally Waugh '034 does not qualify as prior art under any other subsection of 35 U.S.C. §102. For example, Waugh '034 is not prior art under 35 U.S.C. §102(a). Because Waugh '034 and the present application have the same inventors, the presently claimed invention was not "known or used by others..." as required to sustain a rejection under 35 U.S.C. §102(a).

In addition, Waugh '034 is not prior art under 35 U.S.C. §102(b). As noted above, the present application is a national phase application corresponding to PCT/US05/07524, which was filed on March 3, 2005, claiming the benefit to priority to U.S. Provisional Application 60/550,015 filed March 3, 2004. Since Waugh '034 was published December 11, 2003, it was not published "more than one year prior to the date of the application for patent in the United States" as required to sustain a rejection under 35 U.S.C. §102(b). Furthermore, none of the other subsections of 35 U.S.C. §102 (i.e., §§102(c); 102(d), 102(g), or 102(g)) apply either. Accordingly, Waugh '034 is not available as prior art under 35 U.S.C. §102, and rejection should be withdrawn.

## H. Waugh '773 Does Not Anticipate the Presently Pending Claims

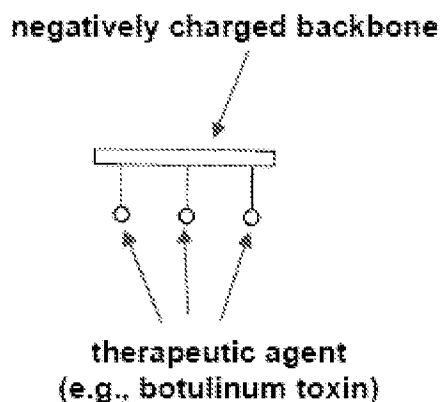
In this section, Applicants discuss International Application No. WO 2002/07773 to Waugh et al. (“Waugh ‘773”), which was not cited by June 11, 2010 Office Action in this case, but was cited during the examination of co-pending U.S. Application No. 11/072,026. In particular, Applicants note that Waugh ‘773 does not anticipate any of the claims in the pending case, because Waugh ‘773 does not disclose a composition where “the carrier and the botulinum toxin non-covalently and directly associate,” as required by the present claims. While Waugh ‘773 mentions that botulinum toxin or BOTOX® can be a cosmeceutical agent or a therapeutic agent (see, e.g., page 15, line 34, or page 16, line 14), both cosmeceutical and therapeutic agents are described as “biological agents” by Waugh ‘773. *See, e.g.,* Waugh ‘773, page 3, lines 32-33, page 15, line 20. Critically, to the extent that “biological agents” are present in the compositions of Waugh ‘773, *they are attached to a negatively charged backbone*. For example, in the “Summary of the Invention” section, Waugh ‘773 states that its compositions comprise “a third negatively charged backbone having a plurality of attached biological agents.” Waugh ‘773, page 3, lines 28-29. Furthermore, this arrangement is illustrated in Figure 1 of Waugh ‘773, an excerpt of which is reproduced below:



As stated in the specification of Waugh '773, Figure 1 shows that the therapeutic agents (e.g., botulinum toxin) are attached to “a short negatively charged backbone”:

In this figure, the components are shown as (1) a solid backbone having attached positively charged groups (also referred to as efficiency groups shown as darkened circles attached to a darkened bar), for example (Gly) $n_1$ -(Arg) $n_2$  (wherein the subscript  $n_1$  is an integer of from 3 to about 5, and the subscript  $n_2$  is an odd integer of from about 7 to about 17) or TAT domains ; (2) a short negatively charged backbone having attached imaging moieties (open triangles attached to a light bar); (3) *a short negatively charged backbone having attached targeting agents and/or therapeutic agents (open circles attached to a light bar)*; (4) an oligonucleotide, RNA, DNA or cDNA (light cross hatched bar); and (5) DNA encoding persistence factors (dark cross hatched bar).

Waugh '773, pp 5-6. In other words, the attachment between the short negatively charged backbone and the therapeutic agents (e.g., botulinum toxin) is represented by the structure associated with reference numeral 3 in Figure 1, a structure which is reproduced below with annotations:



Waugh '773 states that the use of negatively charged backbones with therapeutic agents and other components allows the formation of complexes with a positively charged backbone without the need to precisely position the therapeutic agent on a particular location on the positively charged backbone:

By placing these components on a negatively charged backbone, the invention obviates the need for attaching components in precise locations on a positive backbone as employed in other strategies (increasing complexity and expense and decreasing efficiency to a level that no successful combination has yet been reported due to steric limitations).

Waugh '773, p. 5. Thus, the formation of Waugh '773's complexes that contain biological agents (such as botulinum toxin) is mediated by the interaction between the positive and negative charges on the positively charged backbone and negatively charged backbone, respectively. Accordingly, Waugh '773 does not disclose a composition where "the carrier and the botulinum toxin non-covalently and *directly* associate," as required by the present claims.

In view of the foregoing, Applicants respectfully maintain that Waugh '773 is not prior art under 35 U.S.C. §102 with respect to the presently pending claims.

#### H. Rejections Under 35 U.S.C. §103

##### 1. Rejections Based on the Combination of Waugh '034 and Hanin

Applicants respectfully traverse the rejection of claims 64-73, 78, 79, 82-85, 94-96, 105-109, 116, 149, and 150 for allegedly being unpatentable over Waugh '034 in view of Hanin. As noted above, Waugh '034 is not available as prior art under 35 U.S.C. §102. Accordingly, Waugh '034 is not available as prior art under 35 U.S.C. §103. See, e.g., MPEP §2141.01, *citing to Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert. denied, 481 U.S. 1052 (1987).

Setting Waugh '034 aside, Applicants turn to Hanin alone and respectfully assert that Hanin does not render the presently pending claims unpatentable. Hanin is directed to a method for determining the effects of clostridial toxins upon a muscle. Nowhere does Hanin teach or

suggest “topically applying to the skin or epithelium of the subject the botulinum toxin in conjunction with an effective amount of a carrier comprising a polymeric backbone having attached positively charged branching groups” as recited, for example, in claim 51. Because Hanin fails to teach or suggest all of the features of the presently claimed invention, Hanin does not render the presently pending claims unpatentable. *See, In re Royka*, 490 F.2d 981, 985 (CCPA 1974).

2. Rejection of Claim 117 Over Waugh ‘034, Hanin, and Waugh ‘100

Applicants respectfully traverse the rejection of claim 117 for allegedly being unpatentable over Waugh ‘034, Hanin, and Waugh ‘100. As noted above, Waugh ‘034 and Waugh ‘100 are not available as prior art under 35 U.S.C. §102. Accordingly, neither Waugh ‘034 nor Waugh ‘100 is not available as prior art under 35 U.S.C. §103. *See, e.g.,* MPEP §2141.01 (*internal citations omitted*).

Setting Waugh ‘034 and Waugh ‘100 aside, Applicants are again left with Hanin alone. As noted above, Hanin fails to teach or suggest all of the features of claim 51. Since claim 117 depends indirectly from claim 51, Hanin also fails to teach or suggest all of the features of claim 117. Accordingly, the rejection of claim 117 under 35 U.S.C. §103(a) should be withdrawn. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

I. Statement of Small Entity Status Revisited

In a previous paper, Applicants claimed small entity status with respect to this application and paid reduced additional claim fees on this basis. However, due to developments in

Applicants' business, Applicants are now a large entity and will henceforth pay fees as a large entity.

**AUTHORIZATION**

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this response to Deposit Account No. 50-3732, Order No. 13720-105071US2.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-3732, Order No. 13720-105071US2.

Respectfully submitted,  
KING & SPALDING, L.L.P.

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